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TOPIC: Combinatorial, Parallel, and Solid Phase Chemistry

TITLE: Ring-Closing Metathesis of Macrocyclic Compounds and Cross-Metathesis of Allyl Esters of Amino Acids Leading to Peptidomimetics

AUTHORS: Tammy K.C. Low and Eric Enholm

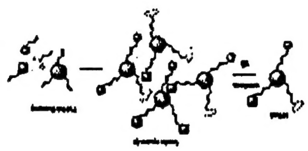
The preparation of a dynamic combinatorial library of peptides using the cross-metathesis of allyl esters of amino acids was examined in a model study. This preliminary investigation employed Grubbs' second generation catalyst for the ring-closing metathesis of unique macrocyclic systems. An N-allyl lactam function, that was part of the large ring, was reacted with allyl esters of amino acids in a cross-metathesis coupling. The reversibility of the reaction, the modified amino acids, and the dynamic biomimetic aspects were all of interest in this study on new types of cyclic peptidomimetics.

Ring-Closing Metathesis of Macrocyclic Compounds and Cross-Metathesis of Allyl Ester of Amino Acids Leading to Peptidomimetics

TAMMY K.C. LOW and ERIC J. ENHOLM
DEPARTMENT OF CHEMISTRY, UNIVERSITY OF FLORIDA, GAINESVILLE 32611

INTRODUCTION

Ring-closing and cross-metathesis reactions are important tools in organic synthesis. The reversibility of cross-metathesis makes it ideal for use in dynamic combinatorial chemistry. In particular, we are interested in generating a library of new cyclic peptidomimetics. The reversibility of the reaction, the modified amino acids, and the dynamic biomimetic aspects are all of interest in this study.



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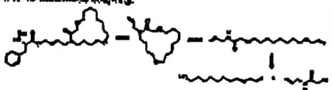

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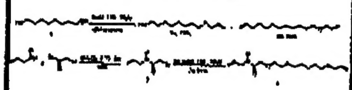
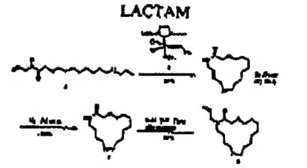
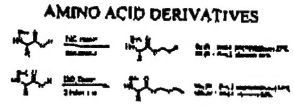


LACTAM



AMINO ACID DERIVATIVES



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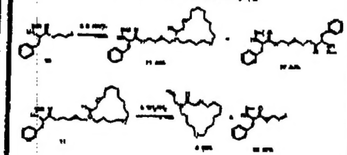
CROSS-METATHESIS



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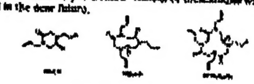
The Model Study has demonstrated the reversibility of the cross-metathesis reaction of an allyl ester of amino acid with N-allyl lactam, a key toward creating a dynamic library. Based on these studies, we are synthesizing N-allyl lactams with various number of "arms" (dimer, trimer, and tetramer). In the dimer studies, a small library of cyclic peptidomimetics was generated. Various templates are now being examined to shift the equilibrium where only one major constituent of the library is formed. Results of these studies will be released in the near future.



ACKNOWLEGEMENTS

Enholm Group Members:
Joel Hennings, Sophie Klein, Ryan Martin, and Kalyan Mondal

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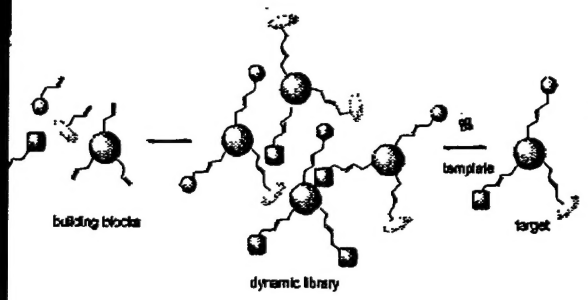

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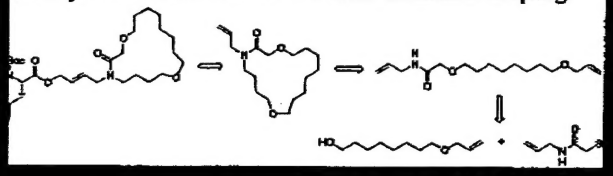

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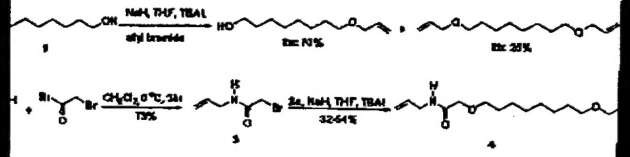

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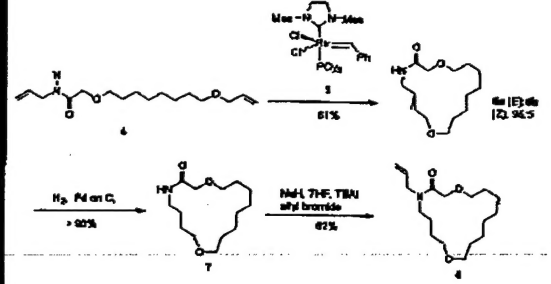

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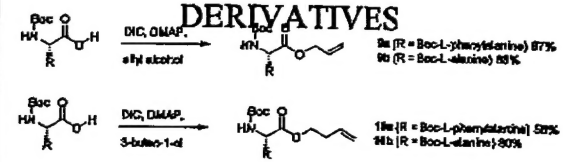
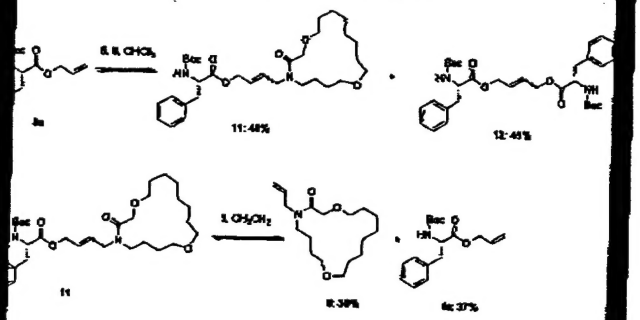


[1] Blackwell H. E. et al. *J. A. Chem. Soc.* 2000, *122*, 58-71
[2] Reichwein, J. F.; Liskamp, R. M. J. *Eur. J. Org. Chem.* 2000, *12*, 2335-2344
[3] Hiraki, H. et al. *Tetrahedron Lett.* 2004, *45*, 1091-1094

CROSS-METATHESIS



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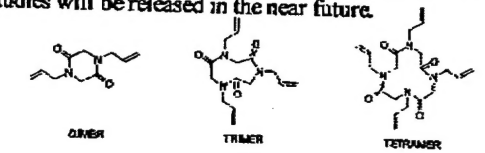

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